Mental Health Perspectives of HIV Infection and AIDS

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Abstract

The human immunodeficiency virus (HIV) epidemic continues to be a major public health problem after more than 30 years of the initial discovery of the infection and the delineation of the routes by which it is spread. Psychiatric disorders play a role in the epidemic by increasing risk behavior for infection and decreasing access to treatment. Many individuals are at increased risk because of addictions, personality vulnerabilities, mood disorders, impulse-control disorders, cognitive impairment, social isolation and disenfranchisement, or other barriers to behaviour change. HIV-infected patients with psychiatric illness may experience great difficulty in modifying risk behaviours. Psychiatric disorders too may adversely impact the treatment of HIV infection primarily through undermining treatment adherence. The same psychiatric disorders that prevented patients from reducing their risk prevent them from obtaining benefit from treatment. Untreated patients with high viral loads are more infectious, leading to an increased potential for spread of the HIV epidemic.

Introduction

HIV was originally recognized through a series of cases of young homosexual men with Pneumocystis carinii pneumonia in the early 1980s in California. Current global statistics suggest that nearly 750,000 infants are born each year with HIV infection, while some estimate that 16,000 new infections occur each

day globally, with one individual being infected about every 10 seconds [1]. AIDS-related stigma and mental disorders are the most common conditions seen in people living with HIV (PLHA). AIDS-related stigma and discrimination impede millions of PLHA from accessing and benefiting from effective prevention and treatment services. Mental disorders are also found to be among the most common problems in the life of PLHA, regardless of gender or race/ethnicity, and can impact their health status, healthcare seeking behaviours, and quality of life. Depression, alcohol use disorders, and neurocognitive disorders are the most prevalent mental problems in this vulnerable population [2]. The purpose of this brief review is to prepare readers who may be unfamiliar with HIV-associated neurocognitive disorders (HAND).

Psychiatric Conditions Associated with HIV

Delirium

Delirium is a state of global derangement of cerebral function. It occurs more frequently in medically ill, brain-injured, or metabolically unstable patients. Prevalence of delirium in HIV-infected populations has been reported to be between 43 and 65 percent. Delirium occurs frequently in patients with advanced HIV infection [3]. Hospitalized patients with AIDS also were found to have increased mortality if delirium complicated their hospital course [4]. The clinical presentation of delirium in HIV patients is the same as it is in non-HIV-infected individuals and is characterized by inattention, disorganized thinking or confusion, and fluctuations in level of consciousness. Emotional changes are common and often

unpredictable, and hallucinations and delusions are frequently seen. The syndrome has an acute or a subacute onset and remits fairly rapidly once the underlying etiology is treated. The cause of delirium should be aggressively sought. Particular considerations in HIV patients include hypoxia with Pneumocystis pneumonia, malnutrition, CNS infections and neoplasms, systemic infections (e.g., mycobacteria, CMV, bacterial sepsis), HIV nephropathy, substance intoxication and withdrawal, medication toxicity, and polypharmacy. Variations in hydration or electrolyte status may also profoundly affect patients with HIV who already have cerebral compromise. HIV infection itself also may produce an acute encephalopathy similar to that reported with CMV [5]. Older age, multiple medical problems, multiple medications, impaired visual acuity, and previous episodes of delirium, patients with HIV-associated dementia are at an increased risk to develop delirium. The differential diagnosis of delirium includes HIV-associated dementia, especially with AIDS mania, minor cognitive–motor disorder, major depression, bipolar disorder, panic disorder, and schizophrenia. Delirium can usually be differentiated from the above conditions based on its rapid onset, fluctuating level of consciousness, and link to a medical etiology.

Treatment consists of three parts. The first and the foremost is the identification and removal of the underlying cause. The second is the reorientation of the patient by maintaining a normal diurnal variation of light cycles, providing orienting stimuli, such as calendars, clocks, and a view of the outside world, and active engagement and reorientation by staff members, family, and friends. The third, if necessary, is the management of behaviour or psychosis. Low

doses of high-potency antipsychotic agents are usually effective. Newer, atypical antipsychotics are currently being used with some success, but those drugs with more anticholinergic activity may worsen the condition. Benzodiazepines should be used with caution as they may contribute to delirium in some patients but are of particular use in alcohol or benzodiazepine withdrawal delirium. Physical restraint may be necessary, if the patient turns violent, however, it should be used only when alternatives are inadequate, because restraint may worsen delirium. If indicated, typical neuroleptic medications should be used at the lowest dosage and for the briefest duration possible. Atypical antipsychotics are generally preferred because of lower risk for EPS. Terminal delirium in HIV, as in other terminal diseases, is much more refractory to treatment.

HIV-Associated Dementia

Early in the AIDS epidemic, some patients presented with rapidly progressing neurocognitive disturbances, leading to an intensive search for etiology. CNS opportunistic conditions and CNS lymphoma were identified, however, a subset of patients remained for which no identifiable pathogen could be found, and it was deduced that HIV itself was the causative factor behind the dementia. Autopsy studies of demented AIDS patients revealed characteristic white matter changes and demyelination, microglial nodules, multinucleated giant cells, and perivascular infiltrates but a marked absence of HIV within neurons. Basal ganglia and nigrostriatal structures are affected early in the dementia process, with diffuse neuronal losses following. Typical late findings indicate an approximate 40% reduction in frontal and temporal neurons. Analyses of CSF

and autopsy material also have shown aberrant production of specific cytokines in patients with HIV-associated dementia [6, 7]. The cumulative prevalence of HIV dementia in the lifetime of an infected adult has been reported to be near 15 percent, although the incidence has decreased by about 50 percent since the introduction of HAART. Its frequency among patients with otherwise asymptomatic HIV infection or with CD4 cell count greater than 500 cells/mm3 is probably less than 5% in a community sample [8].

Clinically, dementia presents with the typical triad of symptoms seen in other subcortical dementias—memory and psychomotor speed impairments, depressive symptoms, and movement disorders. Initially, patients may notice problems with reading, comprehension, memory, and mathematical skills. But since these symptoms are subtle, they may be overlooked or discounted as fatigue and illness. The Modified HIV Dementia Scale is a very useful bedside screen and can be administered serially to document disease progression. Later, patients were found to develop more global dementia, with marked impairments in naming, language, and praxis. Motor symptoms are also often subtle in the early stages and include occasional stumbling while walking or running; slowing of fine repetitive movements. Impairments on tests of psychomotor speed in patients at time of AIDS diagnosis with no memory complaints have been shown to predict development of HIV-associated dementia up to 2 years later. Parkinsonian features are common in HIV-associated dementia, and clinical correlates between HIV and Parkinsonism too have been identified [9]. Apathy is a common early symptom of HIV-associated dementia. A frank depressive syndrome also commonly develops, typically with irritable mood and anhedonia instead of sadness

and crying spells. Sleep disturbances and weight loss are common. HIV-associated dementia is rapidly progressive, usually ending in death within 2 years. HIV-associated dementia has been suggested as a strong risk factor for suicide [10]. In the Multicentre AIDS Cohort Study [11], the proportion of cases of HIV-associated dementia in patients with CD4 cell counts between 201 and 350 cells/ mm3 was higher in 1996–1998 compared with the figures in early 1990s. This suggests that screening for HIV-associated dementia should be extended to patients with CD4 cell counts less than 350 cells/mm3 [11]. The extended survival that antiretroviral regimens have offered patients may also increase their vulnerability to developing dementia rather than dying secondary to other fulminant complications [12].

Initial open-label studies using AZT (Zidovudine, Retrovir) showed promising results, with patients improving on neuropsychological tests [13]. Studies and reports of antiretroviral treatment of HIV-associated dementia relate the clinical improvements of patients, the reversal of confluent MRI signal abnormalities in deep white matter, and a normalization of cerebral metabolites associated with the progression of dementia after 9 months of treatment with HAART. However, controversy exists regarding the duration of treatment and outcome of dementia. Some studies suggest a dose–response relationship between duration of exposure to zidovudine and dementia-related morbidity [14]. Other evidence shows a temporary relation between zidovudine and stability of improvement of cognitive function [15]. The long-term effect of HAART on the course of HIV-associated dementia remains undetermined, with some evidence of ongoing HIV-related cognitive damage despite more than 3 years of potent antiretroviral treatment [16]. Risperidone and clozapine have been described in case reports of HIV-associated dementia with psychosis, with significant improvement in psychotic symptoms and few EPS [17]. Quality care for patients with HIV-associated dementia is to ensure an optimal HAART regimen and to treat associated symptoms aggressively. Depression can be treated with standard antidepressants, and, in some cases, methylphenidate or other stimulants may be useful in treatment of apathy.

Minor Cognitive–Motor Disorder

HIV-associated dementia is a late-stage disorder, whereas minor cognitive-motor disorder (or mild neurocognitive disorder) is a less severe syndrome observed in earlier HIV infection. Patients with this disorder may present with a singular minor complaint, such as taking longer to read a novel, dysfunction when performing fine motor tasks such as playing the piano, an increased tendency to stumble or trip, or making more mistakes when balancing the check book. Minor cognitive-motor disorder is now regarded as part of the spectrum of HIV-associated dementia, and its description in the literature has fallen out of use. Prevalence data for minor cognitive-motor disorder are variable, often suggesting up to 60% prevalence by late-stage AIDS. Prevalence in earlier stages is not well defined. Whether minor cognitive-motor disorder inevitably leads to HIV-associated dementia is uncertain. It appears that some patients may continue to have minor problems, whereas others will progress to frank dementia. HAART may be of some benefit in slowing down progression, but this conclusion is confounded by

a lack of understanding of factors that lead some patients to progress while others remain static.

Major Depression

Depression is a significant problem in HIV/AIDS. The question of whether the incidence or prevalence of major depression increases in case of HIV-infected patients has been a controversial topic [18]. The estimated prevalence of major depressive disorder (MDD) in HIV-infected patients has been reported to be 19%–43% [19]. High rates of major depression have been found in homosexual men and patients with substance use disorders. Depression has a negative impact on adherence with medical treatments, quality of life, and finally, treatment outcome. Major depression is a risk factor for HIV infection by virtue of its effect on behavior, intensification of substance abuse, exacerbation of self-destructive behaviors, and promotion of poor partner choice in relationships [20]. HIV aggravates the risk of developing major depression through a variety of mechanisms, including direct injury to subcortical areas of brain, chronic stress, worsening social isolation, and intense demoralization. The Multicentre AIDS Cohort showed that rates of depression increased 2.5 fold as CD4 cells declined to fewer than 200/mm3 just before patients developed AIDS, suggesting that lower CD4 cell counts predict increased rates of depression [21]. This suggest that HIV is a causal factor in depression and that depression is a causal factor in HIV transmission and its morbidity, making the patients with these disorders a treatable vector for the HIV epidemic and suggesting an important role for mental health care in HIV treatment and prevention. High prevalence rates of suicide have been reported among HIV-infected patients [22].

Factors associated with HIV and suicide include depression, hopelessness, alcohol abuse, poor social support, low self-esteem, and a history of psychiatric disorder.

The diagnosis of major depression in the HIV clinic is complicated by the high frequency of depressive symptoms that are associated with chronic illness, significant losses and isolation, comorbid neurological illness, comorbid substance use, and the use of many medications that can alter mental function. Patients complaining of depressive symptoms may have their depression overlooked or discounted due to the presence of a plethora of other diagnoses. Nonspecific somatic symptoms are often the result of depression rather than HIV infection in patients who do not have concurrent medical illness. Fatigue has also been found to be associated with depression and not HIV disease progression. Worsening of fatigue and insomnia at 6 month follow-up was highly correlated with worsening depression but not CD4 count, change in CD4 count, or disease progression by CDC category. Depression is most likely to be missed when symptoms are attributed to HIV-associated dementia, fatigue, demoralization and disenfranchisement, wasting syndrome, or substance abuse. Care should be taken in distinguishing between major depression and demoralization (i.e., adjustment disorder) in patients with HIV. Approximately, one-half of the patients presenting to an urban HIV clinic with complaints of depression were found to have demoralization alone [22]. The ability to report feeling fairly normal when distracted from thinking about the precipitating event or circumstance causing distress is a hallmark of demoralization. HIV-related medical conditions and medications can cause depressive symptoms. CNS infections

such as toxoplasmosis, cryptococcal meningitis, lymphoma, and syphilis are associated with high rates of depressive symptoms. Drugs, such as efavirenz, interferon, metoclopramide, clonidine, propranolol, sulfonamides, anabolic steroids, and corticosteroids, have been reported to produce depression. These depressive symptoms often respond to withdrawal of the offending drug.

Treatment with HAART was associated with significant improvements in symptoms of depression, but did not necessarily have a causal relationship [23]. Pharmacotherapy is the mainstay of treatment for major depression. Several studies have demonstrated the efficacy of various antidepressant agents in HIV patients, but no single antidepressant has been found to be superior in treating HIV-infected patients as a group. As is the case with all depressed patients, nonadherence is the most common reason for ineffective drug treatment, and adverse effects are the most common reason for nonadherence. Since HIV-infected patients are likely to be more sensitive to side effects, antidepressants should be started at sub-therapeutic dosage and raised slowly. Psychostimulants also have been evaluated for treatment of fatigue, cognitive impairment, and depression in patients with HIV. An important issue is the interaction of antidepressants and HAART medications. As depression is associated with reductions in adherence to HAART, the risks of untreated depression must be measured against those of potential medication interactions. Psychotherapy is an important and integral part of the treatment of major depression. Treatment with medication plus psychotherapy has been shown to be more effective for patients than either modality alone. Supportive psychotherapy, group therapy and cognitive-behavioural therapy (CBT)

have all shown to be effective in patients of HIV with depression.

Bipolar Disorder

Bipolar disorder is a condition in which patients experience episodic alterations in mood that causes disorder. Manic episodes are associated with increased rates of substance abuse and impulsive behavior, and there has been speculation that bipolar disorder may be a risk factor for HIV infection. To date, there has been no unequivocal evidence to prove that bipolar illness directly increases the risk for HIV infection. Patients with pre-existing bipolar disorder may experience exacerbations because of the stresses of HIV illness. Perhaps the additional presence of CNS inflammation or degeneration secondary to HIV may also help worsen underlying bipolar disorder, and new-onset mania could be a result of the organic insult itself. The prevalence of mania has been found to be increased in patients with AIDS when compared with the general population [24]. Some have suggested that mania should be subdivided into primary and secondary types, with patients who have the secondary type showing close temporal proximity to an organic insult, no history of illness, essentially negative family history, and late age at onset [25]. Secondary mania includes cases those coming up due to HIV brain disease itself [26], those due to antiretroviral drugs [27], and those due to other HIV-related conditions (e.g., cryptococcal meningitis) or medications. Concurrent or subsequent cognitive impairment has been reported among cases of HIV-related mania. The secondary mania associated with HIV was found to be associated with low CD4 cell count [28], often lower than 100 cells/mm3. The incidence of secondary mania,

like that of HIV-associated dementia, appears to have declined after the widespread use of HAART [29]. AIDS mania is usually quite severe in its presentation and malignant in its course. AIDS mania seems to be more chronic than episodic, with infrequent spontaneous remissions, and usually relapses with cessation of treatment.

Treatment of secondary HIV or AIDS mania has not been systematically studied to date, and the optimal treatment remains unclear. Reports often have indicated a particular resistance of manic symptoms to treatment. Others have noted few differences in response in the treatment of secondary HIV mania compared with bipolar disorder [28]. The treatment of mania in early stage HIV infection is not substantially different than the standard treatment of bipolar disorder. It relies on the use of mood-stabilizing medications, particularly, lithium salts and the anticonvulsants valproic acid, lamotrigine, and carbamazepine and antipsychotic agents, now more commonly atypical agents. These medications decrease manic symptoms and may prevent recurrence.

Schizophrenia

Literature on patients with severe and chronic mental illnesses, primarily schizophrenia and bipolar disorder, reports HIV prevalence rates between 2% and 20% in both inpatient and outpatient samples [30]. There is no evidence that HIV infection causes schizophrenia, but there are data to show that schizophrenia contributes to behaviors that may lead to HIV infection. Substance abuse is very common in schizophrenic patients, including during sexual activity [31]. Patients with schizophrenia have significantly less knowledge about HIV infection and transmission than persons without schizophrenia [32]. Even increased knowledge about HIV in schizophrenic patients may not lead to decreased risk behaviors [33]. Suicidality is found to be at an increased level in patients with both schizophrenia and HIV infection. For all these reasons put together, clinicians should evaluate schizophrenic patients for risk behaviors and for their knowledge about HIV. The principles of treatment for HIV-infected patients with schizophrenia follow the same basic principles as any other patient with schizophrenia, namely, control of symptoms with medications and psychosocial support and rehabilitation.

Substance Abuse and Addiction

Triple diagnosis refers to a patient with a dual diagnosis (substance abuse and psychiatric disorder) who also has HIV, and such patients are overrepresented in HIV treatment. Substance abuse is a primary vector for the spread of HIV in the case of those who use intravenous drugs along with their sexual partners and those who are disinhibited by intoxication or driven by addiction to unsafe sexual practices. Injection drug use is obviously a primary risk factor for contracting HIV by needle sharing. Addiction and high-risk sexual behavior have been linked across a wide range of settings. Alcohol intoxication also can lead to risky sexual behaviors by way of cognitive impairment and disinhibition [34]. Substance abuse may augment HIV replication in the CNS and increase HIV encephalopathy in early AIDS. The medical sequelae of chronic substance abuse accelerate the process of immunocompromise and amplify the burdens of HIV infection. Injection drug users are at higher risk for developing bacterial infections such as pneumonia, sepsis, and endocarditis.

Tuberculosis, sexually transmitted diseases (STDs), viral hepatitis, co-infection with human CD4 cell lymphotrophic virus, and lymphomas also occur more commonly in injection drug users with HIV than in other patients with HIV. HIV infected injection drug users are at higher risk for fungal or bacterial infections of the CNS. Alcohol abuse is immunosuppressive and increases risk for bacterial infections, tuberculosis, and dementia. Heroin may worsen HIV-associated nephropathy.

Posttraumatic Stress Disorder

Posttraumatic stress disorder (PTSD) and its symptoms occur at greatly increased rates in HIV-infected patients [35]. PTSD increases the likelihood of engaging in destructive behaviors such as alcohol and other drug abuse, sexual promiscuity, or prostitution. PTSD is of particular concern in HIV treatment and research as it may engender or exacerbate HIV risk behaviors and worsen health outcomes. PTSD from early life trauma may predispose an individual to engage in high-risk sexual or drug behavior. On the other hand, risk behaviors such as prostitution and drug abuse increase exposure to trauma and thus the likelihood of developing PTSD. Finally, HIV infection itself may be the cause of PTSD. Rates of PTSD in response to HIV infection are higher than those in response to other debilitating illnesses [36], including cancer [37]. Persons at risk for HIV and HIV-infected individuals should be routinely screened for PTSD and psychiatric comorbidities, with treatment targeted accordingly.

Personality Issues

The fact that knowledge of HIV and its transmission is insufficient to deter individuals from engaging in HIV risk behaviors suggests that certain personality characteristics may enhance a person's tendency to engage in such behaviors. Such individuals, who report high rates of sex and/or drug risk behaviors, include HIV-infected drug users, patients presenting at HIV primary care clinics for medical treatment, and HIV-infected men who have sex with other men. This persistence of high-risk behaviors among individuals who are HIV-infected is a disturbing trend in the HIV epidemic. Educational approaches for risk reduction have proved ineffective for individuals with certain personality characteristics [38]. Effective prevention and treatment programs for HIV-infected individuals must consider specific personality factors that render them vulnerable to practicing risky behaviors that further endanger their health as well as the health of others.

Clinical experience makes us believe that unstable extroverts are the most prone to engage in practices that place them at risk for HIV. Patients present with this blend of extroversion and emotional instability. These individuals are preoccupied by, and act on, their feelings, which are labile, leading to unpredictable and inconsistent behavior. Most striking is the inconsistency between thought and action. Regardless of intellectual ability or knowledge of HIV, unstable extroverts can engage in extremely risky behavior. Their primary goal is to achieve immediate pleasure or removal of pain, regardless of circumstances. As part of their emotional instability, they experience intense fluctuations in mood. Unstable extroverts are more likely to pursue sex promiscuously. Unstable extroverts are more vulnerable to alcohol and drug abuse. They are drawn to alcohol and drugs as a quick route to pleasure. They are also more likely to become injection drug users.

Stable extroverts are also present oriented and

pleasure seeking; however, their emotions are not as intense, as easily provoked, or as mercurial. They may be at risk because they are too optimistic or sanguine to believe that they will become infected with HIV. Unstable introverts are anxious, moody, and pessimistic. Typically, these patients seek drugs and/or sex not for pleasure, but for relief or distraction from pain. Stable introverts account for the rest of the patients. These patients, with their controlled, even-tempered personalities, are least likely to engage in risky or hedonistic behaviors. Typically, these individuals are HIV positive as a result of a blood transfusion or an occupational needle stick.

Prevalence rates of personality disorders among HIV-infected patients (19%–36%) and individuals at risk for HIV (15%–20%) are high and significantly exceed rates found in the general population (10%) [39]. The most common personality disorders among HIV-infected patients are anti-social and borderline types [40]. Anti-social personality disorder is the most common and is a risk factor for HIV infection [40].

Adherence is especially challenging in HIV, which carries all of the components of low adherence—long duration of treatment, preventive rather than curative treatment, asymptomatic periods, and frequent and complex medication dosing [41]. Average rates of nonadherence to antiretroviral therapy range from 50 to 70 percent, with adherence rates of <80 percent associated with detectable viremia in a majority of patients. Clinical experience suggests that non-adherence is more common among our extroverted or unstable patients, the same personality characteristics that place them at risk for HIV. Missing doses of HAART can increase the chance of development of HIV resistance. Cognitive-behavioral approach is most effective in treating patients who present with extroverted and/or emotionally unstable personalities.

HIV-Specific Psychotherapeutic Issues

There are a number of specific circumstances where psychosocial interventions help in HIV-infected patients. These are:

1. Pretest, test, and posttestcounseling issues
2. Risk behavior reduction in patients at risk or infected with HIV
3. Issues of partner notification in patients infected with HIV
4. Impaired patients with issues of capacity and competence
5. HAART adherence issues

Studied interventions have included stress management and relaxation techniques, group counseling, education, cognitive training, negotiation skills training, psychotherapy directed at emotional distress reduction, relapse prevention models of high-risk behavior reduction, education directed at eroticizing safer sex, assertiveness training, and peer education in bars.

Adherence Counseling

The single most important factor regarding outcome of HIV treatment is the patient's ability to adhere to a prescribed regimen. The literature on adherence indicates that there are four groups of factors that affect adherence: environmental factors, treatment factors, illness factors, and patient factors. Environmental factors include medication cost, work schedules, transportation, housing issues, and lack of supportive relationships. Missed appointments are a strong predictor of treatment failure, suggesting that any factor that interferes with patients coming for treatment will interfere with adherence [42].

Treatment factors include the type of medication and amount of pill burden. Perceived side effects also correlate with poor adherence and can prevent patients from taking all required doses in an attempt to prevent adverse consequences. Illness chronicity, symptoms, and curability also affect adherence. Lifelong illnesses have the highest degree of nonadherence, as do illnesses that are asymptomatic, because the patient is unable to feel any benefit or effect from taking a medication. Patient factors associated with nonadherence including dementia, depression, psychosis, personality factors, and substance use. The current literature on HIV medication adherence focuses on technical interventions such as pill box and timer reminders, less complex pharmacological interventions, decreased pill burdens, and increased access to care. A growing literature examines psychosocial interventions, relationship with care providers, case management, and psychiatric disorders as barriers to adherence.

Conclusion

The interrelationships between HIV/AIDS and psychiatric disordres are myriad and complex. Psychiatric disorders can be seen as vectors of HIV transmission, through associated high-risk behaviors. They also complicate the treatment of HIV infection. Use of psychotropic medications with HAART involves drug–drug interactions. Few anti-retroviral drugs like efavirenz and ritonavir can cause psychiatric symptoms and altered blood levels of psychotropic medications. Comorbid psychopathology– including major depression, schizophrenia, addictions, personality vulnerabilities such as unstable extraversion, and the effects of traumatic life experiences are highly prevalent in patients with HIV/AIDS. Each of these problems has the potential to sabotage treatment for HIV infection and its many complications. There is a profound shortage of information and availability of psychiatric care in HIV clinics. Comprehensive care for HIV patients should involve screening for psychiatric conditions and adequate management of the same. By doing so, even the most difficult patients can be successfully treated.

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